

Access to pharmaceuticals: the EU picture

Prepared by Brian Godman



**Karolinska
Institutet**



1. Introduction

2. Potential ways forward

3. Conclusion

Prices and access to new medicines are key issues in Europe balanced against considerable unmet need

- There are growing concerns among European payers about the rising costs of new medicines especially for cancer and those for orphan diseases, exacerbated by the emotive nature of these disease areas – balanced against continued unmet need
- This is despite the limited health gain of most new medicines coupled with the low cost of goods of most including biological medicines. Alongside this, CEE countries are struggling to fund biological medicines for immunological diseases at Euro 1000 – 1500/ patient/ month – although easier with biosimilars
- This is leading to developments including new models for new medicines incorporating new pricing approaches for orphan diseases, calls for greater transparency in price negotiations with concerns with MEAs, development of European collaborations and position statements (EURODIS), and greater use of low cost generics and biosimilars

Prescrire believes very few new drugs and indications are advances - most minor advance or similar to existing drugs/ indications

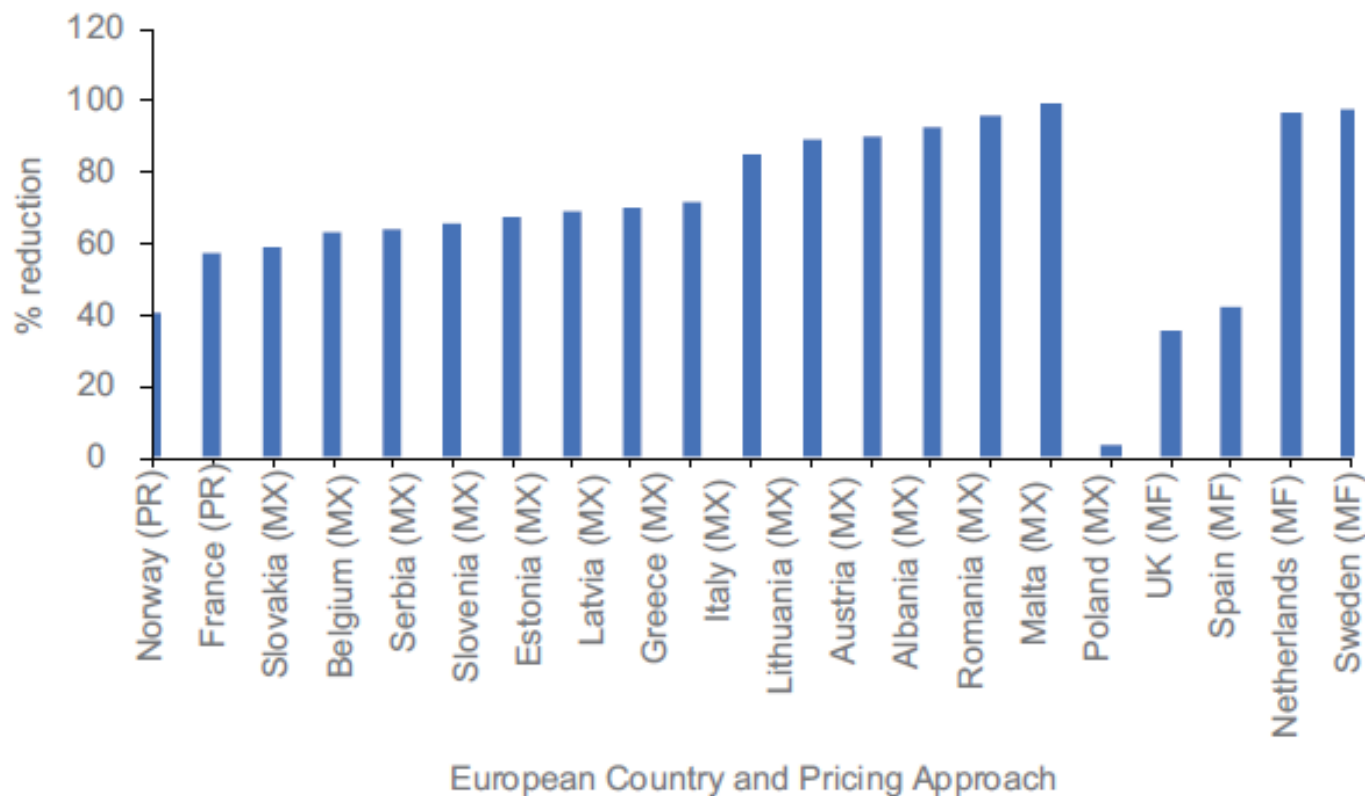
Prescrire ratings	2006	2008	2010	2012	2014	2015
Innovative drug/ real therapeutic advance	2	0	1	1	3	3
Offers an advantage (modest)	8	6	3	3	5	5
Possibly helpful	31	25	22	14	15	15
Nothing new	69	57	49	42	35	43
Not acceptable including safety concerns	17	23	19	15	19	15
Judgement reserved - usually due to insufficient data	8	9	3	7	10	6
Total	135	120	97	82	87	87

In 2017 out of 92 medicines only 1 real advance and 2 with modest benefits

This is seen also for new cancer medicines causing concern with ever increasing prices

- Of the 12 drugs approved by the FDA for various cancers in 2012:
 - ❑ 9 were priced at more than US\$10,000/patient/ month
 - ❑ Only 3 prolonged survival, 2 by less than 2 months
- Of the 7 targeted therapies for renal cell carcinoma approved in the US between 2005 and 2012:
 - ❑ all improved progression-free survival (PFS) by typically 3 to 6 months
 - ❑ However, minimal or no impact on overall survival at a cost of US\$70,000 to US\$140,000/ patient annually
- Recent studies have shown that the cost of goods of some new cancer medicines can be as low as 1% of the selling price. New medicines for hepatitis C also have low cost of goods resulting initially in gross profit expectations of over 99.9% in Europe

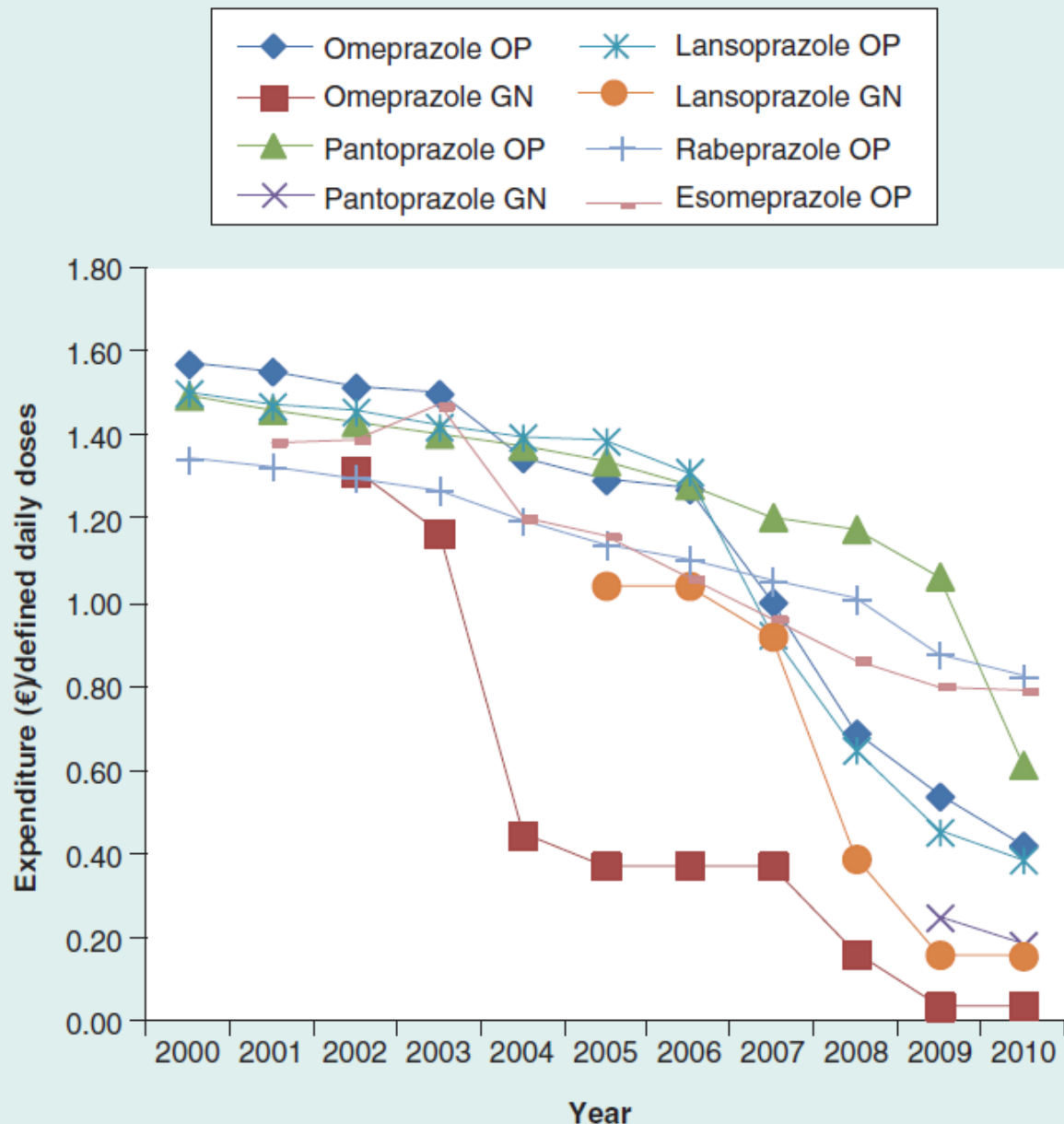
Figure 3: Percentage reduction in imatinib prices (generic prices in 2017 versus originator prices in 2013) among European countries where this data was available



In addition, UK prices 89.1% reduction in March 2018 following greater competition.

MF: Market forces; MX: mixed approach; PR: prescriptive pricing.

The cost of goods of new cancer medicines can be very low as seen with imatinib with generics



This mirrors low prices for other oral generics e.g. generic omeprazole in the Netherlands (similarly for generic simvastatin) with their preference pricing policy

Appreciable price reductions are also likely with biosimilars in time with e.g. Abbvie offering HUMIRA at a 89% discount in the Netherlands to try and prevent biosimilar entry

Continuing high prices for new cancer medicines despite often limited health gain – driven by the emotive nature of the disease area - is resulting in these headlines

BMJ 2017;359:j4543 doi: 10.1136/bmj.j4543 (Published 2017 October 05)

Page 1 of 4



FEATURE

DRUG REGULATION

Cancer drugs: high price, uncertain value

A study published in The BMJ this week shows how most new cancer drugs are failing to deliver any clinically meaningful benefit. It's time for Europe to raise the evidence bar before market approval, finds **Deborah Cohen**

Potential ways forward include establishing minimum threshold levels for granting premium prices for new cancer medicines

Proposed minimum criteria have centred on 3 months additional survival – first proposed in the UK in 2000

British Journal of Cancer (2000) 83(10), 1268–1273

© 2000 Cancer Research Campaign

doi: 10.1054/bjoc.2000.1406, available online at <http://www.idealibrary.com> on IDEAL®

New treatments for advanced cancer: an approach to prioritization

JSJ Ferguson¹, M Summerhayes², S Masters¹, S Schey² and IE Smith³

¹Lambeth, Southwark and Lewisham Health Authority, 1 Lower Marsh, London SE1 7NT; ²Guy's, King's and St Thomas' Joint Cancer Centre, London SE1 7EH;

³The Royal Marsden Hospital NHS Trust, Downs Road, Sutton, Surrey SM2 5TP, UK

Utilisation of the ESMO-MCBS in practice of HTA

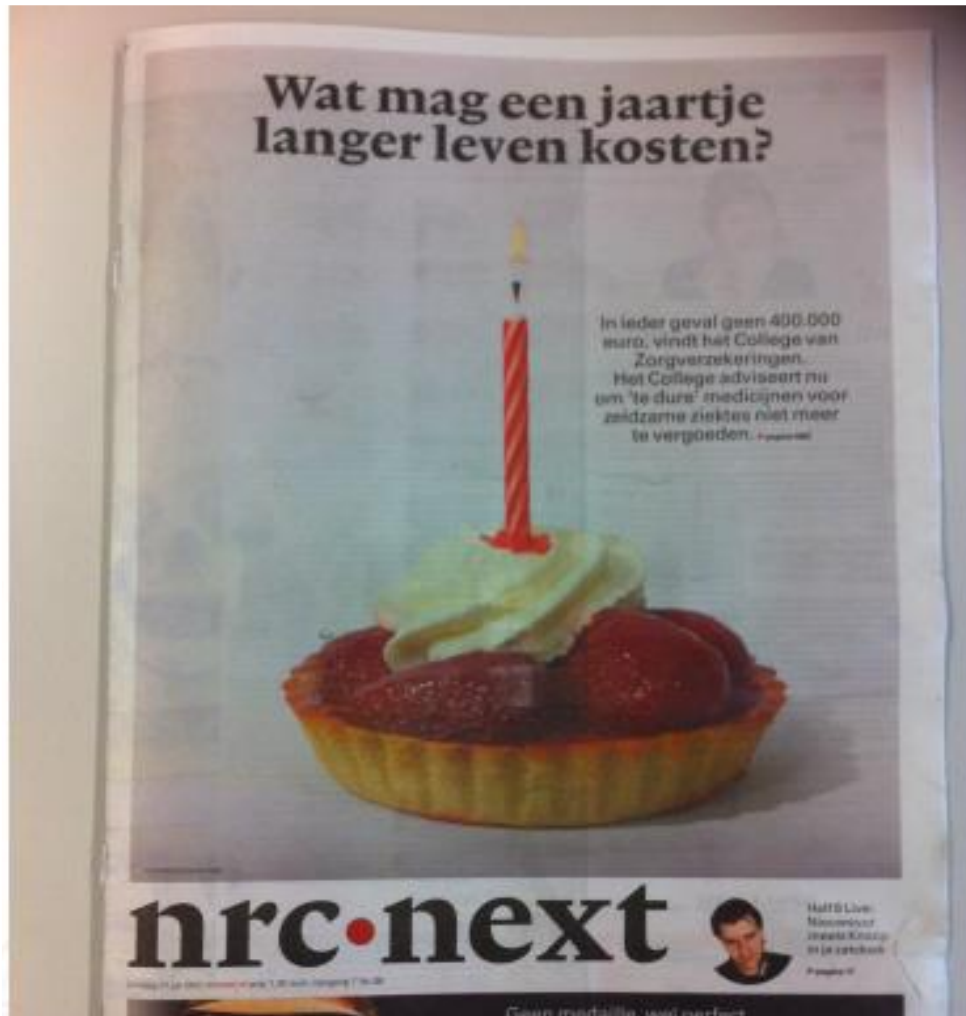
We also recently critiqued the ESMO criteria for valuing new cancer medicines and proposed a number of adaptations based on overall survival to take account of increasing budgetary issues and concerns with surrogate markers such as objective response rates and PFS – especially in solid tumours

Concerns with ever increasing prices for new medicines for orphan diseases is resulting in publications such as Luzzatto et al in the Lancet in 2018. However an appreciable number have annual costs less than Euro1000/ patient/ month

Outrageous prices of orphan drugs: a call for collaboration

Lucio Luzzatto, Hanna I Hyry*, Arrigo Schieppati, Enrico Costa, Steven Simoens, Franz Schaefer, Jonathan C P Roos, Giampaolo Merlini, Helena Kärridinen, Silvio Garattini, Carla E Hollak, Giuseppe Remuzzi, on behalf of the Second Workshop on Orphan Drugs participants*

www.thelancet.com Vol 392 September 1, 2018



Pressure from the media in the Netherlands resulted in pressure on the MoH to ignore the advice of the reimbursement agency about funding enzyme replacement therapy for Fabry's disease (up to €3.3 million incremental cost / QALY) and up to €15million for alglucosidase alfa to treat Pompe's disease

Such situations cannot continue for the sustainability of European healthcare systems – leading to the TVF for new biological medicines for orphan diseases

Patient and media pressures have resulted in Orkambi (lumacaftor/ivacaftor) being funded despite concerns

- The same pressures are continuing with lumacaftor/ivacaftor for CF patients who are homozygous for the F508del mutation (45%). After 24 weeks, there was a statistically significant improvement in ppFEV1 (2.6–3 - 4%) – however seen as uncertain clinical significance - and pulmonary exacerbations were less (although not significant). In addition, 73% with Orkambi failed to achieve an absolute improvement of at least 5% in ppFEV1
- In the 96-week extension study (PROGRESS trial), the mean absolute change in ppFEV1 remained above baseline in patients continuing with Orkambi - however, the difference from baseline was no longer statistically significant (and certainly limited clinical significance)
- This may though mask appreciable benefits in some patients
- In view of concerns with the overall extent of health gain coupled with requested prices – Orkambi was initially rejected by NICE. Similarly rejected in Canada by CDR at an estimated ICER of Ca\$4.8million/ QALY when compared to current standards of care
- However in England following pressure and additional discounts - the decision has recently been reversed – following the lead in Scotland

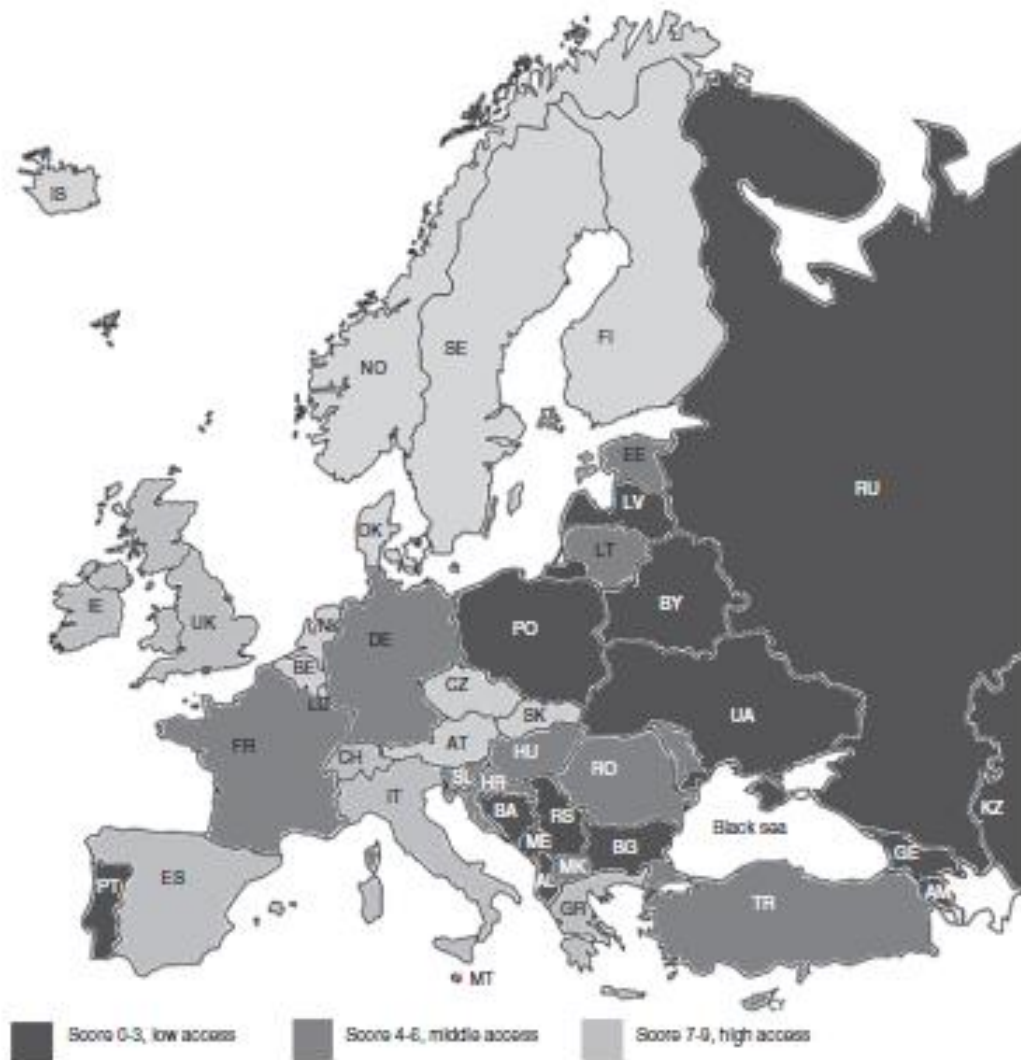


Orkambi was recently funded in England following appreciable pressure from the media and patients.

Some patients though have appreciably benefited from Orkambi

There is an ongoing class action in Canada for Orkambi as a result of differences in funding between organisations

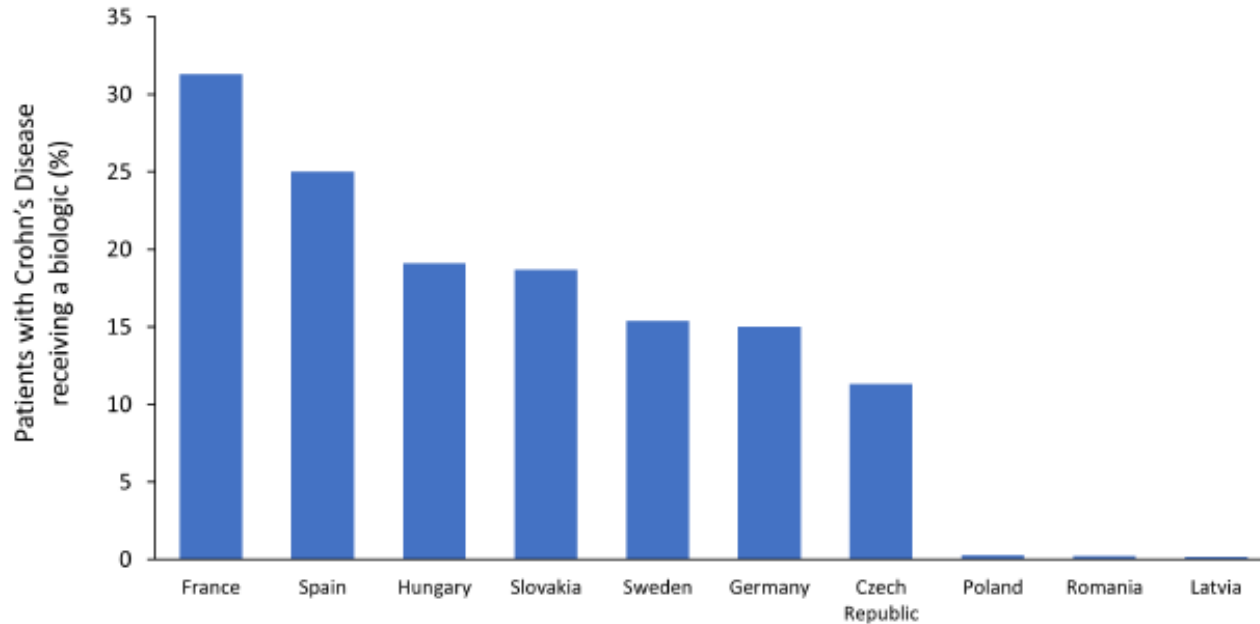
- **'Class action suit raises questions about how Canada funds drugs to treat rare diseases'** – headline in Vancouver Star 26 July 2018 – with Chris MacLeod launching a class action suit seeking \$60 million in damages on behalf of patients refused coverage of Orkambi
- While the costly medication is covered by some health plans (Private) in Canada - not approved for funding by provincial/ federal governments due to lack of cost effectiveness (ICER of Ca\$4.8mn)
- However, MacLeod said Orkambi can be life-changing for some patients and that they have the right to this medicine under Section 7 of the Charter, which guarantees that "everyone has the right to life, liberty and security of the person"
- Likely to see similar media/ activities in other countries to try and enhance funding for Orkambi despite the costs and benefits involved
- Nobody though is challenging the gross profit being made by the companies involved with the NPV of these medicines estimated at \$33billion in 2013 – with royalty expenses and production costs averaging just 12.6% of revenues. This needs to change for the future sustainability of healthcare systems



There has been variable use of biological medicines to treat patients with rheumatoid arthritis across Europe in recent years

Putrik et al in 2014 showed considerable variation depending on issues of socioeconomic status, co-payments and disease severity

High scores were associated with good access



There is also considerable variation in the use of biologicals in patients with inflammatory bowel disease across Europe driven again by issues of access and affordability

Kostic et al in Serbia also found limited use of biologicals for IBD due to high patient co-payments

1. Introduction

2. Potential ways forward

3. Conclusion

Potential ways forward include better planning and co-ordination by payer groups, MCDAs and realistic prices

- Improved pro-active planning by health authorities starting with Horizon Scanning as well as greater co-operation over HTA assessments (e.g. Nordic group) will help. This includes early dialogue with pharmaceutical companies
- Companies actively reducing the disconnect between the potential health gain of a new medicine and their price – especially if considerable uncertainty exists (reducing with initiatives such as TRUST4RD) – enhanced with the recent experience with Olaratumab across Europe
- Greater transparency regarding requested prices to aid discussions – especially with ageing populations across Europe. MCDAs have also been proposed to assist with pricing negotiations as an alternative to cost/ QALYs/ ICERs by MOCA
- Researching potential new funding approaches – and greater co-operation among payers building on current networks

Improved managed entry of new medicines is growing in Europe

Time lines Pre- and Peri- Launch

**2-3 years before likely
EMA authorisation**

**1 year from
EMA
authorisation**

**EMA
authorization**

**Reimbursement
(National and
Regional)**

**Horizon scanning (in
association with others)**

**Evaluation risk
sharing arrangements**

**Additional
regional
restrictions**

**Assess budget impact based
on likely patient numbers
and perceived 'value' with
key groups. Start
discussions on patient
registries (if pertinent)**

**Guidelines on use with
key physician groups
especially where concerns
– possibly addressing PR**

Peri and post-launch activities

**Communication programmes
with key stakeholder groups**

**Patient follow-up on
effectiveness and safety in
practice using registries or
EHRs**

**Evaluate adherence to agreed
guidance/ guidelines/ restrictions.
Initiate additional demand-measures
if needed**



Stockholm County Council and now across Sweden has a well developed system for Horizon Scanning, feeding into funding and procurement decisions and follow-up post launch. In Stockholm, horizon scanning activities feed into annual forecasts for medicines across disease areas to help with planning

Addressing some of the concerns with managed entry agreements and different confidential discounts being offered across European countries

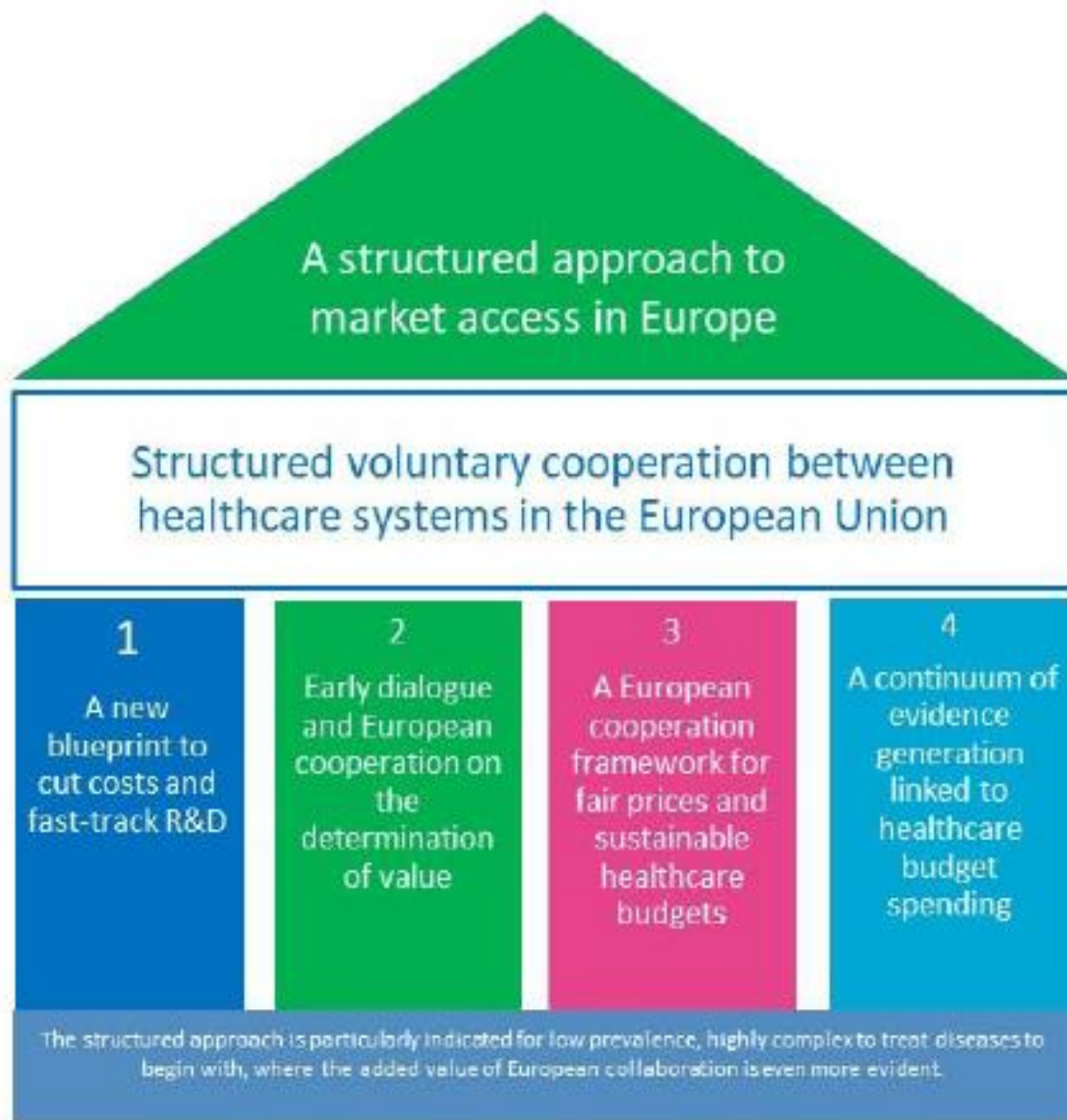
WHO Resolution “*Improving the transparency of markets for drugs, vaccines and other health-related technologies*” adopted during the 72nd session of the World Health Assembly in May 2019.

- **proposed by IT, co-sponsored by other countries including a number of countries signatory to the Valletta Declaration;**
- **implementation of the recommendations.**



The Transparent Value Framework (TVF) was developed by key stakeholders as part of the MoCA-OMP project following the situation in the Netherlands to provide guidance for the pricing new medicines for orphan diseases and is still being evaluated. Other MCDAs have also been proposed as potential ways forward

Criterion	Lower Degree	Medium Degree	High Degree
Available Alternatives/ Unmet Need, including non-pharmaceutical treatment options	yes, new medicine does not address unmet need	yes, but major unmet need still remains	no alternatives except best supportive care - new drug addresses major unmet need
(Relative) Effectiveness, Degree of Net Benefit (Clinical Improvement, QoL, etc. vs. side effects, societal impact, etc.) relative to alternatives, including no treatment.	incremental	major	curative
Response Rate (based on best available clinically relevant criteria)	<30%	30-60%	>60%
Degree of Certainty (Documentation)	promising but not well-documented	plausible	unequivocal



Such approaches are also included in EURORDIS' Vision that they would like to see 3 to 5 times more new rare disease therapies approved per year, 3 to 5 times cheaper than today, by 2025 to benefit all European citizens with rare diseases especially those in CEE countries

1. Introduction

2. Potential ways forward

3. Conclusion

New systems and co-operation are needed to ensure fair pricing for medicines to maintain UHC for all in Europe

- Ongoing developments with the various pan-EU country co-operations - combined with greater proactivity pre-launch through to post launch - will enhance objectivity in pricing and funding negotiations for new medicines and their place in therapy. In time, this should help accelerate funding for new medicines that truly benefit patients and limit funding for new premium priced medicines with limited health gain
- We are also likely to see further pricing models to enhance the opportunity for all European citizens to benefit from new valued medicines. At the same time, encourage greater use of generics and biosimilars without compromising care to ease budgetary pressures
- In addition, potential re-evaluation of the role/ value of patented medicines once the comparator medicine used in negotiations becomes available as a generic/ biosimilar

Thank You

Any Questions!

Brian.Godman@ ki.se;
Brian.Godman@liverpool.ac.uk;
Brian.godman@strath.ac.uk;
briangodman@outlook.com